REMARKS

Claims 1-3, 5-10 and 12-14 were previously and are still pending and under examination in this application. No new matter has been added.

Rejections Under 35 U.S.C. §103

The Examiner rejected claims 1-3, 5-10 and 12-14 under 35 U.S.C. §102(a) as being unpatentable over Cruz, U.S. patent 4,148,664 ("Cruz") in view of Mechanic, U.S. patent 5,332,475 ("Mechanic")

As to claims 1-3, 6-10 and 13-14, the Examiner asserts that Cruz discloses "a fibrous collagen hemostatic product having a bulk density in a range of 1.5 -3.7 lbs/ft^3 required for a hemostatic product, and a neutral (pH =7) or acidic (pH<7) or alkaline (pH>7) treatment solution for an un-denatured collagen." The Examiner also asserts that Cruz also discloses avoiding "denaturalization" [sic, denaturation] of the collagen. According to the Examiner, Cruz "does not disclose explicitly using water as a treatment solution for suspending collagen[t] fibrils as recited in the claim. However, Mechanic –'475 (col. 2, lines 42-68; col. 3, ll. 1-2 col. 4, ll. 19-53) discloses using collagen fibrils or finely ground bovine skin collagen in a cross-linking process not subjected to an acid dissolution to make collagen fiber/fabric/matrix to be used inside a human being as an implant. Inherently, the product to be used inside a human body must have been sterilized."

The Examiner further asserts that "Mechanic (col. 4, lines 54-64; claim 2 lines 1-8) discloses proteinaceous material/collagen fibril(s) being suspended in an aqueous media such as water (having a pH in a range of 6.8 to 8.6) to avoid denaturalization of the collagen." The Examiner alleges that "Mechanic - '475 explicitly teaches avoiding denaturalization [sic, denaturation] of collagen fibrils (col. 4, lines 19-50) by suspending collagen fibrils in water (col. 4, lines 50-64)." According to the Examiner, "[i]t would have been obvious to one of ordinary skill in the art at the time of the invention to use water as a treatment solution for a hemostatic product as disclosed by Cruz-'664 in view of Mechanic-'475 as using water would minimize denaturalization [sic, denaturation] of the collagen fibrils."

Applicant respectfully disagrees and requests reconsideration in view of the Declaration submitted herewith and in view of the following remarks. The instant invention is directed to methods of forming a collagen product and the products produced thereby, which involve suspending collagen in water and avoiding acid dissolution. In a preferred embodiment, a collagen fiber is prepared by a process which involves extruding a collagen slurry containing collagen fibrils into a dehydrating bath. The instantly claimed hemostatic collagen fabric is formed of collagen fibers of the invention.

Applicant herewith submits a Declaration by Dr. Surendra Batra in support of the following argument. Cruz teaches a fibrous collagen "having hemostatic and adhesive properties sufficient to join together severed biological surfaces." Batra Declaration at ¶5. Cruz teaches treating water-wet collagen with ethanol to remove water, converting the collagen to an ionizable partial salt in the presence of ethanol and dehydrating with ethanol. Batra Declaration at ¶5. Cruz teaches that drying may also be effected by vacuum drying. Batra Declaration at ¶5. The recovered dry collagen of Cruz is subjected to deaggregation to form a mass having a bulk density of not more than 8 pounds per cubic foot and a surface area of at least 1 square meter per gram (see, for example, Abstract and column 1, lines 36 – column 4, line 49 and Examples). The drying process described by Cruz produces a dry collagen that is at least partially cross-linked. Batra Declaration at ¶6. Cross-linking of collagen reduces its suspendability and reduces its ability to form a slurry in water. Batra Declaration at ¶6. Because of its reduced suspendability in water one of ordinary skill in the art would not have a reasonable expectation of success in using the collagen taught by Cruz to obtain the instantly claimed hemostatic collagen fabric. Batra Declaration at ¶7.

Even assuming, for argument's sake, that one of ordinary skill in the art would have had a reasonable expectation of success in using the collagen taught by Cruz in the instant invention, which the Applicant disagrees with for the reasons stated above, the additional teachings of Mechanic do not cure the deficiencies of the primary reference of Cruz namely, suspending collagen in water. Applicant disagrees with the Examiner that Mechanic teaches suspending collagen in water as instantly claimed.

The Mechanic patent was cited as the basis for claim rejections during prosecution of the parent of the instant application (Serial No: 09/209,723; filed: December 11, 1998; "Collagen Hemostatic Fibers", now U.S. patent 6,361,551 B1). The parent application involved forming collagen suspensions in water. Applicant successfully overcame the rejections using a declaration by inventor Stephen Eldridge and related documents presented during prosecution of the parent application. In previous responses, Applicant argued that Mechanic does not teach using non-buffered water or non-buffered aqueous media to suspend collagen. The same arguments are applicable here and some of these arguments are briefly reiterated. For the sake of brevity, the Examiner is referred to the prior responses (filed on May 17, 2004, February 17, 2005, May 26, 2005, and October 24, 2005) for further elaboration on Applicant's arguments and reasoning.

Mechanic teaches an improved method for cross-linking collagen products and the collagen products produced thereby. Mechanic describes a process for cross-linking and stabilizing proteinaceous material such that the end product of this process retains "the mechanical properties of the pre-treated material, that is, they remain supple and pliant" (Col. 3, lines 52-61). In order to accomplish this objective, Mechanic teaches that the proteinaceous material to be cross-linked is immersed in an aqueous media that is suitable for processing in accordance with the Mechanic invention. Mechanic states (beginning at Col. 4, line 50, emphasis added):

> "The proteinaceous material to be photoxidized is then immersed, dispersed, or suspended (depending upon its previous processing) in an *aqueous media* for processing in accordance with the present invention. Suitable media for immersion of the proteinaceous material (for purposes of convenience, the word "immersion" shall be considered to include suspension and/or solubilization of the proteinaceous material) include aqueous and organic buffer solutions having a neutral to alkaline pH, preferably a pH of about 6.5 and above because of the denaturation caused by acid pH. Particularly preferred are buffered aqueous solutions having a pH of from about 6.8 to about 8.6.

Thus, Mechanic teaches the importance of dispersing proteinaceous material in buffer solutions having a neutral to alkaline pH. Mechanic does not teach or suggest lyophilizing a suspension of a proteinaceous substance to form a hemostatic fabric comprising collagen fibrils wherein the fibrils have been suspended in water.

In contrast to Mechanic, Applicant's claimed invention is directed to the use of collagen fibrils in water for fabricating a collagen fabric with retention of hemostatic activity. Although water itself is a pH neutral liquid, collagen fibrils are acidic and, when collagen is suspended in water, the pH of the resulting suspension is in the range of about pH 3.04 to about pH 3.09 (see the Eldridge Declaration, a copy of which was submitted with Applicant's response filed on May 17, 2005). Thus, although Mechanic broadly discloses placing proteinaceous material in an aqueous medium that could be water, a suspension of collagen in water would not result in a suspension having a neutral to alkaline pH as set forth in Mechanic for the reasons stated above.

Mechanic also discusses the disadvantages of dispersing collagenous material in aqueous acid solution (Col. 2, lines 42-49):

> ...Acid has the well known effect of denaturing the protein comprising the collagen fibril. It is, of course, the three-dimensional structure of the proteins comprising the collagen fibril which imparts to the fibril the unique properties of collagen; change that structure and the protein cannot interact in the manner needed to give rise to those properties.

There are no further teachings in Mechanic patent to suggest using water to suspend collagen or any other "proteinaceous material". All of the Examples in Mechanic involve suspending collagen in aqueous buffered solutions. All of the claims in Mechanic require performing the cross-linking step in an aqueous buffer such that the pH is maintained at between about 6.8 and about 8.6 or in a buffered medium having a neutral to alkaline pH.

Mechanic is a divisional of U.S. Patent No. 5,147,514 ("Mechanic '514"). Although the two Mechanic patents identify water as a medium for dispersing proteinaceous material, neither of the Mechanic patents describes any further use of water to prepare a collagen suspension. Indeed, the Mechanic '514 file history is consistent with Applicant's interpretation of the

Mechanic patents as teaching the need for a buffered medium in order to maintain the integrity of collagen fibrils. For the sake of brevity, the Examiner is referred to the responses filed by the Applicant on May 17, 2004 and February 17, 2005 for a summary of the Mechanic '514 file history. The Mechanic patents and their file histories are public documents which should be considered in their entirety in assessing the Applicant's pending claims.

In view of the foregoing, one skilled in the art would conclude that although Mechanic includes water as an aqueous medium into which proteinaceous material can be dispersed, the Mechanic patents file histories indicate the importance of placing collagen in a buffered medium because a below neutral pH jeopardizes the integrity of the collagen fibrils.

As stated above, a suspension of collagen in water has an acidic pH. A collagen suspension (in water) having an acidic pH is contrary to the teachings of the Mechanic patents. Thus, Mechanic teaches away from suspending collagen in water.

In view of the forgoing remarks and the Declaration submitted herewith by Dr. Bartar, Applicant respectfully requests that the Examiner reconsider and withdraw the rejection of claims 1-3, 6-10 and 13-14 as obvious over Cruz in view of Mechanic.

As to claims 5 and 12, the Examiner asserts that Cruz and Mechanic disclose a hemostatic collagen product having substantially all the limitations in the instant claims except for a hemostatic agent. According to the Examiner, "[i]t is well known to incorporate a hemostatic agent to a collagen product such a fabric/matrix/pad to enhance hemostatic effect" and that "[i]t would have been obvious to one of ordinary skill in the art to incorporate a hemostatic agent to the MECHANIC collagen product so as to enhance the hemostatic effect of the MECHANIC collagen product."

Applicant respectfully traverses the rejection. In view of the arguments presented above, claims 1 and 8 are not obvious. Claims 5 and 12 which further depend from claims 1 and 8 respectively, should, therefore, also be non-obvious. Accordingly, Applicant kindly requests withdrawal of the rejection of claims 5 and 12 under 35 U.S.C. 103.

CONCLUSION

In view of the foregoing remarks, Applicant respectfully requests reconsideration and withdrawal of the rejection of claims. This application should now be in condition for allowance. A notice to this effect is respectfully requested.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time.

If there is a fee occasioned by this response, including an extension fee, that is not covered by an enclosed check, please charge any deficiency to Deposit Account No. 23/2825.

Respectfully submitted,

Torgerson et al., Applicant

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